REMARKS/ARGUMENTS

With this amendment, claims 43 and 46 are pending. Claims 1-42, 44-45, and 47-51 are canceled without prejudice. For convenience, the Examiner's rejections are addressed in the order presented in a January 24, 2008, Office Action.

I. Status of the claims

Claims 43 and 46 are amended to recite "consisting of," rather than "comprising." Support for these amendments is found throughout the specification, for example, at Table 2 on page 48. These amendments add no new matter.

II. Priority claim

According to the Office Action, the priority date of the application is its filing date, April 8, 2004. The claims to recite a β1,4-N-acetylgalactosaminyl (GalNAc) transferase polypeptide encoded by a nucleic acid that can be amplified by primers that bind to the 3' and 5' end of the *C. jejuni* LOS locus. The present application is a continuation application of U.S. Patent Application No. 10/303,128, filed November 21, 2002, which is a divisional application of U.S. Patent Application No. 09/816,028, filed March 21, 2001, which is a continuation-in-part of U.S. Application No. 09/495,406, filed January 31, 2000, which claims the benefit of U.S. Provisional Application No. 60/118,213, which was filed on February 1, 1999. Support for active β1,4-GalNAc transferase proteins is found in the priority document, the '213 application at page 35, lines 6-8 and SEQ ID NO:6. Thus, in view of the pending claims and the disclosures in the related applications, the priority date of the application is February 1, 1999.

III. Rejections for non-statutory obviousness-type double patenting

Claims 43 and 46 are rejected as allegedly unpatentable under the judicial doctrine of obviousness type double patenting over claims 1-7 of US Patent No. 6,723,545. In order to expedite prosecution of this application, Applicants submit a terminal disclaimer of the

term of a patent granted on the instant application over a US Patent No. 6,723,545. Applicants note that the filing of a terminal disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection. *See*, MPEP §804.02. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 43 and 46 are rejected as allegedly unpatentable under the judicial doctrine of obviousness type double patenting over claims 1-6 of US Patent No. 7,238,509. In order to expedite prosecution of this application, Applicants submit a terminal disclaimer of the term of a patent granted on the instant application over US Patent No. 7,238,509. Applicants note that the filing of a terminal disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection. *See*, MPEP §804.02. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 43 and 46 are rejected as allegedly unpatentable under the judicial doctrine of obviousness type double patenting over claims 1-6 of US Patent No. 7,169,593. In order to expedite prosecution of this application, Applicants submit a terminal disclaimer of the term of a patent granted on the instant application over US Patent No. 7,169,593. Applicants note that the filing of a terminal disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection. *See*, MPEP §804.02. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 43 and 46 are provisionally rejected for alleged obviousness type double patenting in view of claims 1-6 of co-pending USSN 10/830,825 (filed April 23, 2004, now allowed). In order to expedite prosecution of this application, Applicants submit a terminal disclaimer of the term of a patent granted on the instant application over a patent granted on U.S. Patent Application No. 10/830,825 (filed April 23, 2004, now allowed). Applicants note that the filing of a terminal disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection. *See*, MPEP §804.02. Accordingly, Applicants respectfully request withdrawal of this rejection.

IV. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 43 and 46 are rejected under 35 U.S.C. §112, for allegedly failing to provide enablement for any β1,4-N- acetylgalactosaminyl (GalNAc) transferase polypeptide encoded by a nucleic acid that can be amplified by PCR using *C. jejuni* genomic DNA and primers comprising SEQ ID NOs:40 and 41. The Office Action does indicate that the specification enables a β1,4-N-GalNAc transferase polypeptide encoded by a nucleic acid that can be amplified by PCR using *C. jejuni* genomic DNA and primers consisting of SEQ ID NOs:40 and 41. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection. Applicants also note that claim 43 is amended to recite consisting of language.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention. *See, e.g.*, *Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

As set forth in the Manual of Patent Examining Procedure (MPEP) § 2164.01, "the test of enablement is not whether any experimentation is necessary, but whether... it is undue." Further, the "fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid

inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971).

The Office Action at page 10 outlines a series of objections to the previously claimed primers that recited comprising language. For example, the specification allegedly does not establish: (A) the structure of all primers comprising SEQ ID NO:40 and 41; (B)how primers comprising SEQ ID NO:40 and 41 can be modified without affecting amplification of the target sequence; (C) the general tolerance of primers comprising SEQ ID NO:40 and 41 to modification; and (D) a rational and predictable scheme for selecting primers that comprise SEQ ID NO:40 and 41. As the claims now recite primers consisting of SEQ ID NO:40 and 41, these objections are now moot. The Office Action also alleges that the specification fails to provide sufficient guidance as to which of "essentially infinite choices" of primer pair is likely to be successful. Again, as the claims recite primers consisting of SEQ ID NO:40 and 41, the choices are not infinite and the guidance provided by the specification is sufficient to meet the enablement requirement.

With regard to the supposed unpredictability of identifying the encoded β1,4-N-GalNAc transferase proteins, Applicants assert again that the specification provides multiple examples of *C. jejuni* β1,4-N-GalNAc transferase amino and nucleic acid sequences. The specification at page 23, line 12 through page 24, line 9 discloses that SEQ ID NO:17 is a β1,4-N-GalNAc transferase protein. The sequence listing provides additional β1,4-N-GalNAc transferase amino acid sequences and encoding nucleic acid sequences at SEQ ID NOs:18-25. The specification also teaches assays to identify active β1,4-N-GalNAc transferase proteins. β1,4-N-GalNAc transferase activity is asserted at, *e.g.*, page 23, lines 13-16 and the specification also provides experimental evidence that the β1,4-N-GalNAc transferase protein of *C. jejuni* strain OH4384 does indeed have β1,4-N-GalNAc transferase activity. *See, e.g.*, specification at page 50, lines 2-4 and page 56, lines 8-14. The β1,4-N-GalNAc transferase substrate is a fluorescent molecule called GM3-FCHASE and the product is called GM2-FCHASE. Figure 4 shows the reaction pathway, including formulas of the acceptor substrates and product, *i.e.*, GM3 and GM2. The β1,4-N-GalNAc transferase protein in figure 4 is referred to as CgtA. The

inventors performed thorough and detailed analysis of the β1,4-N-GalNAc transferase reaction products, *i.e.*, fluorescently labeled FCHASE molecules, to confirm that the recited activity is correct. NMR analysis of the product is disclosed at page 57, lines 1-4 and table 4. Additional mass determination of the product is disclosed at page 67, line 8 through page 69, line 2. Thus, the specification provides disclosure of the reaction conditions to assay β1,4-N-GalNAc transferase activity and verification that transfer of GalNAc from a donor substrate to an acceptor substrate does occur.

The Office Action also alleges that undue experimentation is required by those of skill to make and use the claimed invention. However, the limitation of primers to primers consisting of SEQ ID NO:40 and 41 necessarily limits the number of β1,4-N-GalNAc transferase proteins that are encoded by a *C jejuni* genome sequence that can be amplified by the primers. And even if the genus of encoded proteins has a large number of members, undue experimentation is not required by those of skill to identify the claimed β1,4-N-GalNAc transferase proteins. The specification demonstrates that those of skill routinely perform large numbers of glycosyltransferase assays. First, the art at the time of filing and the specification provide methods to efficiently assay thousands of proteins for glycosyltransferase activity. These assays can be scaled up even further. For example, the specification discloses a screening strategy used to clone the nucleic acid encoding the CstI protein, a α2,3 sialyltransferase, from *C. jejuni*. Specification at page 47, lines 11-30 and page 52, lines 16-26. The inventors made an expression library of chromosomal DNA from a *C. jejuni* strain and used to transform *E. coli*. They picked 2600 library colonies and combined them into pools of 100 and then assayed each of the 26 library pools. Thus, the initial screening step required only 26 enzymatic assays to screen 2600 library colonies. Out of 2600 library colonies the inventors were able to quickly identify 2 clones with enzymatic activity. Pooled assay screens of this type are standard and have been used for many years. Thus, using pooled samples, the number of initial assays can be reduced by 100 or 1000 fold. Similar techniques can easily be used by those of skill to identify functional β1,4-GalNAc transferase proteins. Thus, undue experimentation is not required to practice the claimed invention.

The specification provides enablement of the amended claims. The specification, as discussed above, discloses sensitive β1,4-N-GalNAc transferase assays that can be used to preliminarily identify *C. jejun*i strains that have a β1,4-N-GalNAc transferase protein encoded by a nucleic acids that can be amplified from the LOS locus of the genome. As discussed in the previous response, the specification demonstrates that large scale screens for glycosyltransferase activity are routinely done by those of skill. These techniques can be used, to screen large numbers of *C. jejuni* strains for activity, or once an appropriate *C. jejuni* strain is identified, can be used during cloning in, *e.g.*, *E. coli* cells, to screen large numbers of candidates for a nucleic acid that encodes a β1,4-N-GalNAc transferase protein. The specification provides primers the consist of SEQ ID NO:40 and 41. Productive amplification using those primers will occur only from the genome of *C. jejuni* strains that have an LOS locus with sequences complementary to the primers. β1,4-N-GalNAc transferase reference nucleic acid and amino acid sequences are also disclosed at SEQ ID NOs:16-25. Computer programs are available to identify related sequences. Again, those of skill can use the β1,4-N-GalNAc transferase assays in the specification to identify proteins with the recited activity. Therefore, the possibilities are not infinite and those of skill can identify the claimed proteins, using at most, routine experimentation.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

V. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 43 and 46 are rejected under 35 U.S.C. §112, because the specification allegedly fails to describe the subject matter of the claims. According to the Office Action, the specification fails to describe the structure of sufficient β1,4-N-GalNAc transferase polypeptides to provide descriptive support for the claimed genus. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

Applicants respectfully traverse the rejection. As currently applied, the specification does comply with US patent law for description of a nucleic acid or amino acid

sequence. The Federal Circuit court of Appeals addressed the description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). An applicant may also show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.*, 66 Fed. Reg. 1099, 1106 (2001).

The specification does provide descriptive support for the full scope of the claimed genus by providing a representative number of species of β1,4-GalNAc transferase amino acid sequences and encoding nucleic acid sequences, *e.g.*, SEQ ID NOs:16-25, and a β1,4-GalNAc transferase assay used to determine whether polypeptides have the enzymatic activity required by the claims. The assay is described at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14. This information is more than adequate to meet the written description requirement, particularly in view of *Enzo*, cited above, recent Board decisions, and the interpretation of the Written Description Guidelines evidenced by the USPTO's own Synopsis of Application of Written Description Guidelines.

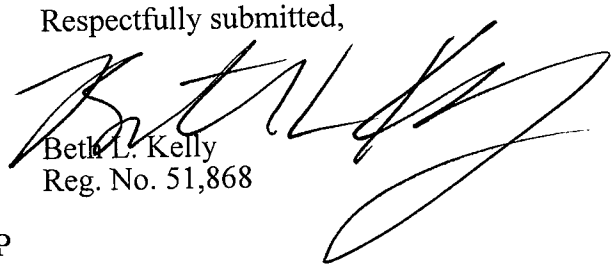
In view of the above arguments and amendments, withdrawal of the rejection for alleged lack of written description is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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